To: Sonawane, Bob[Sonawane.Bob@epa.gov]; Bussard, David[Bussard.David@epa.gov]
From: Caldwell, Jane
Sent: Tue 9/1/2015 2:36:44 AM
Subject: FW: Reassessment [ie-downgrading] of MTBE cancer potency considering modes of action for MTBE and its metabolites
MtBE Cancer Potency-Industry-Bogen-CritRevTox Aug 2015.pdf

FYI

From: Huff, James (NIH/NIEHS) [G] [mailto:huff1@niehs.nih.gov]
Sent: Thursday, August 27, 2015 6:03 PM
To: fiorella belpoggi <belpoggif@ramazzini.it>; morando soffritti <soffrittim@ramazzini.it>; frank mirer <fmirer@hunter.cuny.edu>; myron mehlman <mehlman@comcast.net>; Caldwell, Jane <Caldwell.Jane@epa.gov>; peter infante <pinfante@starpower.net>; ron.melnick@gmail.com; kmb@sciencecorps.org; Ellen Silbergeld <esilber2@jhu.edu>; Dunnick, June (NIH/NIEHS) [E] <dunnickj@niehs.nih.gov>; Lunn, Ruth (NIH/NIEHS) [E] <lunn@niehs.nih.gov>; peter infante <pinfante@starpower.net>; jsass@nrdc.org; bucher@niehs.nih.gov; Birnbaum, Linda (NIH/NIEHS) [E] <birnbaumls@niehs.nih.gov>
Subject: Reassessment [ie-downgrading] of MTBE cancer potency considering modes of action for MTBE and its metabolites

Hi

Wow, one of our favorite INDUSTRY journals coupled with a favorite INDUSTRY shill group.

J

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Reassessment of MTBE cancer potency considering modes of action for MTBE and its metabolites

Kenneth T. Bogen1 and Jacqueline M. Heilman2
1*Exponent Health Sciences, Oakland, CA, USA, and* 2*Exponent Health Sciences, Washington, DC, USA*

Abstract

A 1999 California state agency cancer potency (CP) evaluation of methyl *tert*-butyl ether (MTBE) assumed linear risk extrapolations from tumor data were plausible because of limited evidence that MTBE or its metabolites could damage DNA, and based such extrapolations on data from rat gavage and rat and mouse inhalation studies indicating elevated tumor rates in male rat kidney, male rat Leydig interstitial cells, and female rat leukemia/lymphomas. More recent data bearing on MTBE cancer potency include a rodent cancer bioassay of MTBE in drinking water; several new studies of MTBE genotoxicity; several similar evaluations of MTBE metabolites, formaldehyde, and *tert*-butyl alcohol or TBA; and updated evaluations of carcinogenic mode(s) of action (MOAs) of MTBE and MTBE metabolite's. The lymphoma/leukemia data used in the California assessment were recently declared unreliable by the U.S. Environmental Protection Agency (EPA). Updated characterizations of MTBE CP, and its uncertainty, are currently needed to address a variety of decision goals concerning historical and current MTBE contamination. To this end, an extensive review of data sets bearing on MTBE and metabolite genotoxicity, cytotoxicity, and tumorigenicity was applied to reassess MTBE CP and related uncertainty in view of MOA considerations. Adopting the traditional approach that cytotoxicity-driven cancer MOAs are inoperative at very low, non-cytotoxic dose levels, it was determined that MTBE most likely does not increase cancer risk unless chronic exposures induce target-tissue toxicity, including in sensitive individuals. However, the corresponding expected (or plausible upper bound) CP for MTBE conditional on a hypothetical linear (e.g., genotoxic) MOA was estimated to be $\sim 2 \times 10^{-5}$ (or 0.003) per mg MTBE per kg body weight per day for adults exposed chronically over a lifetime. Based on this conservative estimate of CP, if MTBE is carcinogenic to humans, it is among the weakest 10% of chemical carcinogens evaluated by EPA.